



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Yakhini, et al.

Serial No.: 09/921,406

Filed: August 2, 2001

For: Classifying Cancers

Confirmation No.: 6019

Group Art Unit: 1642

Examiner: Gary B. Nickol

Docket No. 10010313-1 (50112-1970)

DECLARATION OF EDWARD R. DOUGHERTY
PURSUANT TO 37 C.F.R. §1.131

Commissioner of Patents
Alexandria, VA 22313-1450

Sir,

I, Edward R. Dougherty, hereby declare that:

1) The invention embodied in the above-identified patent application is directed to methods for classifying cancers.

2) I am advised that the United States Patent and Trademark Office has rejected one or more claims presently pending in the above-identified patent application based, at least in part, upon Bittner, et al. *Molecular classification of cutaneous malignant melanoma by gene expression*. Nature; Vol. 46 pp. 536-40; 3 August 2000 (herein, *Bittner*). I am further advised that the effective priority date of the *Bittner* publication is August 3, 2000.

3) The invention, however, as embodied in the claims of the present invention was completed by me and my co-inventors Amir Ben-Dor, Michael Bittner, Zohar Yakhini, Yidong Chen, Nicholas M. Sampas, and Paul Metzler in this country prior to August 3, 2000. Specifically, the invention was "completed" by virtue of reduction to practice prior to the

August 3, 2000 priority date of the *Bittner* publication.

4) As evidence that the present invention was so characterized by reduction to practice, Exhibit "A" is attached hereto.

5) Exhibit "A" is a copy of an email sent from co-inventor Michael Bittner to co-inventors of the present application that has attached thereto a draft manuscript of the *Bittner* reference. The manuscript attached to the email of Exhibit A is in substantially the same form as the published manuscript. The email of Exhibit A predates the *Bittner* reference, and includes details of the methods described in part or in whole at least in independent claims 1, 4, 26, and 28 (with like features contained in respective dependent claims as well). Dates and sensitive information (*e.g.*, email addresses) have been redacted in the document in accordance with applicable USPTO rules.

6) The actual manuscript attached to the email of the Exhibit A is not included in Exhibit A because it is not in an electronic form that can be accessed by the Applicants at this time. The co-inventor Michael Bittner is no longer employed by the National Institutes of Health, and therefore is not able to access the electronic records that contain the manuscript.

7) As further evidence that the present invention was reduced to practice prior to publication of the *Bittner* reference, Exhibit "B" is attached hereto.

8) Exhibit "B" is a copy of the PowerPoint[®] presentation that was developed by at least one of my co-inventors. The PowerPoint[®] presentation predates the *Bittner* reference, and includes details of the methods described in part or in whole at least in independent claims 1, 4,

26, and 28 (with like features contained in respective dependent claims as well). In particular, the graph of the gene expression patterns on Slide 5 of the document is identical or substantially similar to FIG. 2B of the instant patent application that identifies genes that discriminate melanoma clusters, including the top 22 genes obtained by multi-dimensional scaling (MDS) analysis ranking genes according to their impact on minimizing cluster volume and maximizing center-to-center inter-cluster distance. In addition, the MDS graph depicted on slide 4 of the document is identical or substantially similar to FIG. 1B of the instant patent application, that shows the clustering of gene expression data, and indicates in particular a MDS three-dimensional plot of all 31 cutaneous melanoma samples showing major clustering of 19 samples, and the remaining 12 outlying samples. One skilled in the art would be able to arrive at the method of claim 1 by reviewing the data and suggestions of the PowerPoint[®] presentation of Exhibit B.

9) Upon information and belief, the Examiner is relying on similar data from the *Bittner* reference as that shown in the document of Exhibit B to reject the instant claims. The inventors of the present application developed the subject matter of the *Bittner* reference prior to the publication date of the *Bittner* reference.

10) As additional evidence that the present invention was reduced to practice prior to publication of the *Bittner* reference, Exhibit "C" is attached hereto.

11) Exhibit "C" is a copy of the invention disclosure submitted to the legal department of Agilent Technologies, the Assignee of record. The invention disclosure includes details of the methods described in part or in whole at least in independent claims 1, 4, 26, and 28 (with like features contained in respective dependent claims as well). In particular, the invention

disclosure discusses on page 1 a method of diagnosing an aggressive form of cancer, based on evaluating expression of WNT5A gene. On page 2 of the invention disclosure, the inventors indicate that the WNT5A's role in melanoma metastasis was suggested in the conclusions of the *Bittner* reference. Therefore, because the inventors are all listed as authors on the *Bittner* reference, the inventors reduced the invention to practice prior to the publication date of the *Bittner* reference. Dates have been redacted in the document in accordance with applicable USPTO rules.

I hereby declare that all statements made herein are of my own knowledge are true and that all statements are made on information and belief and are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

9/16/05
Date

Edward R. Dougherty
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